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TOBACCO INDUSTRY RESEARCH COMMITTEE
150 EAST FORTY SECOND STREET
NEW YORK 17, N. Y.

Application For Research Grant

Date: 20 February , 1959

1. Name of Investigator: H. R. Pratt-Thomas, M.D.

2. Title: Professor of Pathology

3. Institution & Address: Medical College of South Carolina
16 Lucas Street, Charleston, South Carolina

4. Project of Subject: Carcinogenesis in the Laboratory Animal: A comparison of species response to standarized sites of application.

5. Detailed Plan of Procedure:

A towering edifice of experimental data relative to animal carcinogenesis has been constructed over the years, but whether this edifice is structurally sound, particularly in regard to its human application is open to question. The mouse and the rat have been the prime targets in these investigative efforts and the skin and subcutaneous tissues the favorite sites of endeavor. After a decade of working with mice as test animals in attempt to evaluate the possible carcinogenic effects of smegma and tobacco tars, it has become apparent that the murine cellular response is very labile (specifically as regards cervical and vaginal epithelium) and that a variety of stimuli of relatively inocuous proportions are capable of producing neoplasms e.g. simple trauma.
Previous Publications:
Heins, Henry C., Dennis, E. J., and Pratt-Thomas, H. R. : The Possible Role of Smegma in Carcinoma of the Cervix. Amer. Jour. Obs. and Gyn. 76: 726-735, October, 1958.
Pratt-Thomas, H. R., Heins, H. C., Latham, E., Dennis, E. J., and McIver, F. A.: The Carcinogenic Effect of Human Smegma: An Experimental Study. Part I: Preliminary Report. Cancer, 9: 671-680, July-Aug., 1956.; Also Biologic Assay of Cigarette Smoke Tars (to be published).

As the premise of carcinogenic effect in man is often supported by such evidence as the production of neoplasms in the laboratory animal, it is extremely important that species variations be taken into consideration so that any carcinogenic effects may be placed in their true perspective.

We propose to utilize groups of different laboratory animals, rabbits, mice, guinea pigs, hamsters, and rats (monkeys also desirable, but expensive and definitely require long term exposure) and to expose each group

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to identical agents by means of the same procedures. We would utilize chiefly intra-vaginal application technique with which we have had a great deal of experience, but plan to use skin and subcutaneous areas as well so that we may employ a greater range of substances without increasing the number of animals to impractical proportions. The agents to be used would include some of the patent polycyclic hydrocarbons, but particular attention would be given to such agents as ethyl alcohol, silver nitrate, paraformaldehyde, simple trauma, xylene, etc. The impression has been gained that mice (at least some strains) will react in a neoplastic fashion to a wide variety of stimulating or irritating agents, provided the stimulus is applied for a sufficient length of time.

6. Budget Plan:

Salaries	$ 7,000.00
Expendable Supplies	800.00
Permanent Equipment	100.00
Overhead (10%)	790.00
Other	000.00
Total	$ 8,690.00

7. Anticipated Duration of Work: 3 years

8. Facilities and Staff Available: H. R. Pratt-Thomas, M.D. (principal investigator) No salary.

Animal quarters and cages are available as well as all the major technical equipment as may be found in a large and well equipped Department of Pathology. Animal caretakers and the technicians who will maintain a regular schedule of the various applications proposed in this work will be the major item of expense. The same technicians will also prepare all the histologic material as it becomes available.

9. Additional Requirements: None.

10. Additional Information (Including relation of work to other projects and other sources of supply):

The publication of the U. S. Department of Health, Education, and Welfare "Survey of Compounds which have been tested for Carcinogenic Activity" Supplement 1, 1957 lends support to some of the proposals and ideas expressed in the formulation of this project. The numerous articles dealing with animal carcinogenesis and the implication, directly or indirectly inferred, of its relation to neoplastic disease in man makes clarification of this problem mandatory.

/s./ H. R. Pratt-Thomas
Director of Project

/s./ L. W. Michaelis
Business Officer of the Institution

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